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Research article

Physicochemical Parameter of Microcrystalline Cellulose and the Most Acceptability in Pharmaceutical Industries

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Abstract

Microcrystalline cellulose (MCC) HiCel™ is native from cellulose, which is manufactured from wood pulp. Microcrystalline cellulose is made by hydrolysis reaction at temperature and pressure in presence of catalyst, which acts as reaction process increment. It is neutralized after completion of hydrolysis and intended to be used as to make microcrystalline cellulose powder. HiCel™ MCC is white crystalline, free flowing powder and medium in particles size. MCC is free flowing with having physical & chemical properties as per limit and widely used as a pharmaceuticals aid for direct compression & wet granulation. MCC is employed for the production of solid dosage form due to its good compressibility, compatibility, and loading capacity of drugs. HiCel™ is very essential for direct compression because of its all parameter support to direct compression.

Key words: Hydrolysis of wood pulp, Study of different grades of HiCel™, Physical and Chemical parameter of microcrystalline cellulose HiCel™

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1. Introduction

Microcrystalline cellulose is native from cellulose [1]. In pharmaceuticals industries most commonly source of microcrystalline cellulose is fibrous wood pulp [2]. Pulp is hydrolyzed under heat and pressure. In hydrolysis cellulose polymers breaks in presence of water and acid. The cellulose polymers in pulp are reduced to small chain polymers or microcrystals. Beta and gamma cellulose, hemicelluloses and lignin are dissolved with acid and water, and separate out during of washing and filtration; pure alpha cellulose neutralized and makes slurry [3]. A large amount of cellulose present in wood pulp [4]. In market MCC HiCel™ grades are used in bulk for solid dosage form, food products and cosmetic's products. Now days it used in manufacturing of cosmetics products such as face powder, creams, lotions and shampoos etc. It is use as fat substitute, thickener and as binder in cosmetics products. MCC HiCel™ broadly use in food product as a stabilizer, anti-caking agent, fat substitute and emulsifier [5][6]. This slurry is dried with the help of spray dryer and makes powder of microcrystalline cellulose HiCel™. Behalf of little change of spray drier

setting made different grads of MCC look like HiCel™ 90M, HiCel™ 50M, HiCel™ XLM, and HiCel™ LP200, these grades are differ-cent behalf of only physical parameters and various grade of HiCel™ MCC mention are in the Table no. 1. Physical parameters are changed grade vise and chemical parameters are mostly same of all grades. There are many grades of MCC HiCel™ used in different formulation for makes different-different solid dosages form which is employed as binder, filler (diluents), lubricant and as a disintegrant [7]. MCC HiCel™ microcrystalline cellulose powder has low bulk density and broad particle size distribution [7].

Table No. 1. Name and application of different grades of HiCel ™ MCC

S.No	Name of Grade	Application
1	**HiCel™ 90M**	Medium particle size standard MCC grades, suit for direct compressible activities.
2	**HiCel™ 50M**	Fine particle standard MCC grades, especially suit for wet granulation and now days used for direct compression also.
3	**HiCel™ 25M**	Very fine particle size grade, gives a pleasant mouth feel, masks better tastes &supports flavors.
4	**HiCel™ 14**	Equal to HiCel™ 12 and with low moisture content, it is used for sensitivity activity
5	**HiCel™ 12**	Coars particle size MCC grade, outstanding flow ability, good compatibility & high binding capacity. Its providing good content uniformity at low weight variation. it can be used with low concentration of fine activity.
6	**HiCel™ LP 200**	It is less Coars particle size than HiCel™ 12 MCC grade, it is excellent flow ability, good compatibility & high binding capacity. Its providing good content uniformity at low weight variation.
7	**HiCel™ XLM 90M**	It is medium particle size with extra low moisture grade MCC, It is used for Water sensitivity activity.
8	**HiCel™ XLM 50M**	It is fine particle size with extra low moisture grade MCC.
9	**HiCel™ XLM 200**	It is large particle size with extra low moisture grade MCC. It is used for good binding with water sensitivity activity,
10	**HiCel™ HD 90 M**	It is medium particle size with high density grade MCC. It is used for improve the weight variation of solid dosage form in direct compression formulation.
11	**HiCel™ HD 50M**	It fine particle size with high density grade MCC. It is used for improve the weight variation of solid dosage form in direct compression formulation

The amorphous regions are more flat to hydrolysis so partial depolymerized by acid hydrolysis results in shorter and more crystalline fragments [8]. Flow ability of powder play a very important role in drug manufacturing process, in tablet

manufacturing process flow ability involved in mixing and compaction, such as powder flow in hoppers is a crucial factor for direct compression excipients in drug manufacturing to achieve constant and weight uniformity of tablets. Flow ability is affected by the physical properties of powder such as particle size, shape, bulk density [9]. Larger particle size is free flowing and smaller particle size (less than 100 µ) is generally cohesive and flat to flow ability problems [9][10]. Small amounts of MCC HiCel™ are able to efficiently bind other materials, especially poorly tablet-able active pharmaceutical ingredients [11]. In wood pulp cellulose chains are packed in layers held together by a cross-linking polymer (lignin) and strong hydrogen bonds. Dissolving pulps contains cellulose, hemicelluloses and lignin are present, and in cellulose contains alpha cellulose range is 92 % to 98 %, beta and gamma present 1% [12].

2. Materials and Methods

Production of microcrystalline cellulose [13][14].

Fibrous Wood pulp is cut in to paces and hydrolyzed with acid (v/v) at temperature and pressure. Then slurry is transfer for washing and filtration after neutralization this wet MCC is further made to slurry (W/v) and is spray dried to evaporate water Flow chart of process is mention in the figure no. 1. Thus final MCC is obtained in powder form which is sifted to remove course material to meet the specified particle size requirements. Microcrystalline cellulose is white free flowing crystalline powder; it is shown in figure no. 2.

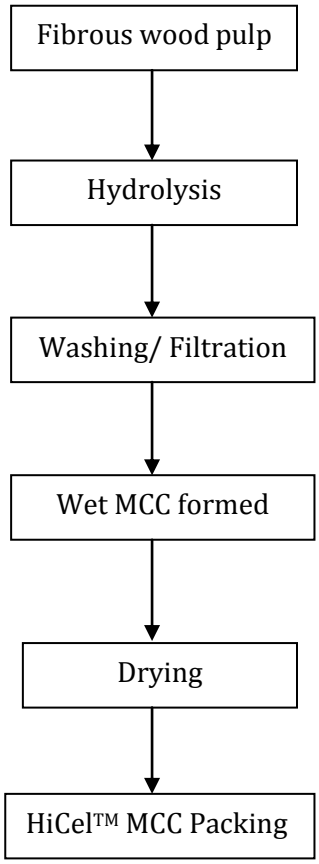

Figure no. 1. Process of production of HiCel ™ MCC

Figure no. 2. HiCel ™Microcrystalline cellulose

Determination of yield value [14]

$$\text{Yield (\%)} = \frac{A}{B} X\ 100 \qquad (1)$$

Whereas; A= weight of obtained microcrystalline cellulose (kg),
B= weight of fibrous wood pulp (kg)

Identification of Microcrystalline celloulose [15]
10 mg of HiCel™ placed on watch glass 3 to 4 drops iodinated zinc chloride solution(20 gram of zinc chloride and 6.5 gram of potassium iodide in 10.5 ml of water, add 05 gram of iodine and shake for 15 to 20 mints (till it dissolved properly). Violet-blue color is changed.

Scanning electron microscopy [16]
Scanning electron microscopy analysis screening was done outside laboratory in (Mumbai).

Average Particle size analysis [17]
Average particle size was analyzed by (Retch-Japanese instrument). Take cleaned mesh sieve with bottom pan and top cover. Check sieve shaker and set mesh sieve with sample being analyzed on sieve jet. Arrange the sieve mesh sequence from top mesh +60, mesh +200 and bottom. Set the amplitude at 1.5 to 2.5 mm, timer at 5 to 7 minutes and interval time at 15 to 20 sec. Weight 10 gm of MCC powder with the help of weight blance (Mettler Toledo,Model no. ML802/A01) and put into top of sieve. After 5-7 minutes take out the sieves and weight the retention separately. Brush the mesh slowly from bottom and collect the all particles retained in between the mesh and consider as retention. Calculate the retention in percentage for each mesh sieve as per the following formula:-

$$\text{Retention \%} = \frac{S(R)}{S(W)} \text{ X } 100 \qquad (2)$$

Whereas; S(R) = Sample retention weight (gram), S(W)= Sample taken weight (gram).

Bulk density [17][18]
Untapped Density: Untapped density was analyzed through graduated measuring cylinder. Take 20 gm of dry MCC powder pours into a graduated A grade 100 ml capacity cylinder slowly from the sidewall. Level the surface of sample in cylinder by slow movement and note down the occupied volume and calculate the untapped density of MCC by using following formula.

$$\text{Untapped density (BD)} = \frac{\text{Weight of powder in gram}}{\text{Occupied volume in mL}} \qquad (3)$$

Tapped Density: Tapped density was anlaysed by using (Electro lab instrument, Model No. ETD1020), measuring cylinder placed in tapped density machine and fixed 100 tapped. After 100 tapped measured the volume of measuring cylinder and calculate the tapped density/porosity of HiCel™ using following formula.

$$\text{Tapped density (TD)} = \frac{\text{Weight of powder in gram}}{\text{Occupied volume in mL}} \qquad (4)$$

Hausner's Ratio [17][18]
The flow of powder was measured by "Hausner ration". Tapped density is divided by true density/untapped density.

$$\text{Hausner's Ratio (H.R)} = \frac{TD}{TB} \qquad (5)$$

Whereas; TD- Tapped density of powder,
TB- Untapped density of powder.

Angle of Repose [17][18]
Pour 30gm of dry MCC through pour on powder flow tester (#10 mesh size), powder comes on the S.S cylinder surface until a pile build on the top of S.S cylinder. Measure the total height (S.S cylinder & pile) by scales. Using following formula find the calculated value this value check natural tangents chart for angle of repose and report angle of repose.

$$\text{Angle of Repose} = \frac{2h}{d} \qquad (6)$$

Whereas; h = height of S.S cylinder,
d = diameter of S.S cylinder.

Moisture content (M.C) [17][18]
Heat the shallow bottle in hot air oven (Model no. PNX-14) at 105°C for 30 minutes after that cool it in desiccators at room temperature. Tare weight the Shallow bottle and take about 1 gm of HiCel ™ MCC in shallow bottle, set oven at 105°C and kept for 3 hours. After 3 hours take out the shallow bottle, allow to cool in desiccators at room temperature. When the shallow bottle is cool take weight again, Calculate moisture content by using the following formula. This procedure repeats three times and takes the average value.

$$(\text{M.C}) = \frac{After\ \ drying\ \ weig\,ht\ of\ \ shallow\ \ bottle - Emp\,ty\ weig\,ht\ of\ \ shallow\ \ bottle}{Sample\ \ \ weig\,ht\ in\ \ gram} \text{ X } 100 \qquad (7)$$

pH and conductivity Analysis [17][18]
Take 5 gm of MCC powder add 40 ml of water mix 20 minutes with the help of glass rod and 20 minutes centrifuge(Remi elektrotechnik, Model no.-Remi-R-8CBL). Retain the supernatant for use analysis the pH by using pH meter (TOSHCON, Model no.-12/H/5563).
Same procedure was followed for conductivity test. Take retain supernatant and check conductivity with conductivity meter (TOSHCON, Model no.-13J1354). Conductivity meter was standardized with a potassium chloride conductivity calibration standard solution.

Degree of polymerization (DOP) [18]
Transfer 1.3 gram of MCC sample accurately weighted to 0.1 mg to a 125 ml conical flask. Add 25 ml of water and 25 ml of 1 M cupriethylen diamine hydroxide solution. Insert the stopper and shake on wrist action shaker until completely dissolved. Transfer an appropriate volume of the solution to a calibrate number 150 Cannon-Fenske or equivalent viscosity meter. Allow the solution to equilibrate at 25 °C ±0.1 °C for not less than 5 minutes. Time the flow between the two marks on viscosity meter and record the flow time, t_1 in seconds. Calculate the kinematic viscosity $(KV)_1$ of MCC taken by the formula: $t_1(K_1)$.
In which, k_1 is the viscosity meter constant. (See viscosity 911 in USP). Obtain the flow time t_2 for a 0.5 M cupriethylene diamine hydroxide solution using a number 100 Cannon-Fenske or equivalent viscosity meter. Calculate the kinematic viscosity $(kv)_2$ of the solvent by the formula, t_2 (k_2). In which k_2 is the viscosity, (η_{rel} of MCC specimen taken by the formula: $(KV)_1$ / $(KV)_2$.

$$\eta = \frac{(\text{KV})1}{(KV)2} \qquad (8)$$

Determine the intrinsic viscosity, (η) c by interpolation, using the intrinsic viscosity table in reference table section. Calculate the DOP, it is denoted by "*P* ".

$$P = \frac{(95)(\eta)C}{Ws\ \{\frac{(100 - \%LOD\ )}{100}\}} \qquad (9)$$

Whereas; WS= weight of MCC powder,
%LOD= Loss on drying of MCC powder

Residue on ignition [18]
Take a crucible and clean properly and Ignite in muffal furnace (Proto-tech, Model no.-PNX-14) at 600 ± 50 °C for 30 minutes. Placed in dissector and allow cool at room temperature. Tare weight of

crucible (C_E) and take sample (S_W) 1 to 2 gram HiCel™ MCC. Again weight the crucible with powder (C_P) and add 2 ml of sulfuric acid, Heat on hot plate (Samiksha, Model No.-SI--12) at 100°C. When white fumes is completely stop than crucible placed in muffal. After 3 hours switch off Muffal furnace and allow cool in dissector at room temperature. If it was not ignite properly again add 2 ml of sulfuric acid and process repeat again. Took weight of crucible with ignite residue (C_I). Residue on ignition was calculated by using formula.

$$S_W = C_P - C_E \quad (10)$$

$$(F_W) = C_I - C_E \quad (11)$$

$$ROI = \frac{FW}{SW} X\ 100 \quad (12)$$

Whereas; C_E = Weight of empty crucible,
C_P = Weight of Crucible with powder (MCC),
S_W = Weight of sample (MCC),
C_I = Weight if ignite residue with crucible,
F_W = Final weight of ignite residue,
ROI = Residue on ignition

Water-soluble substances (WSS) [18]
Properly clean, the evaporating dish(ED), and heat in hot air oven for 30 minutes, allow cool it in desiccators at room temperature. Took tare weight (AE) of evaporating dish. Weighed accurately 5 gram sample MCC powder (AP) and added 80 ml of water, stirred with glass rod till 10 minutes then filter by using filter paper (Whatman no.42) with the help of vacuum pump in to a vacuum flask. Transferred the filtrate to a tarred evaporating dish (ED), evaporated on water bath (Samiksh, Model No.-EI-13) and dry at 105 0C for about 1 hour. Cool evaporating dish in desiccators at room temperature. When it was cool take weight of ED (Ad). Found out the WSS value by using below formula. Same procedure was repeated for blank value. In blank only water was used, there was no other solvent used. Blank value (Bv) was calculated by using formula.

$$S_W = A_P - A_E \quad (13)$$

$$A_F = A_D - A_E \quad (14)$$

$$WSS = \frac{AF - BV}{SW} X\ 100 \quad (15)$$

Whereas; A_E = Weight of empty evaporating dish (ED),
A_P = Weight of evaporating dish with sample (MCC),
S_W = Weight of Sample MCC,
A_D = after drying weight of evaporating dish,
A_F = Final weight of residue,
B_V = Blank value.

3. Results and Discussion

Yield: The yield of dissolving wood pulp is 90 to 92 % w/w. yield of three different batches mention in table no.3. Dissolving wood pulp contain high proportion of alpha cellulose, alpha cellulose is shiny white color. Yield was totally depending on grades and types of wood pulp.

Scanning electron microscopy: Morphology of HiCel™ microcrystalline cellulose powder was studied through Scanning electron microscopy. The particles sizes were analyzed in micrometer, photomicrograph shown in figure no.3. Microcrystalline cellulose fibers were observed to be uniform in size and spherical in shape.

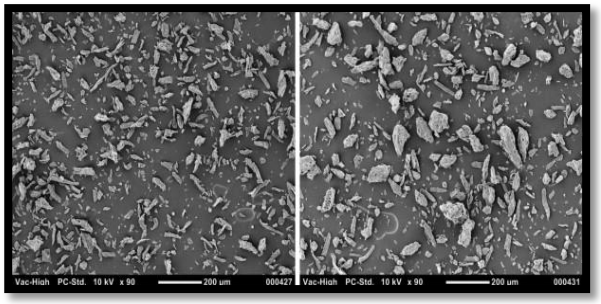

Figure no. 3. Scanning electron micrographs (SEM) of HiCel™ 50M (left) and HiCel™ 90M (right)

Physicochemical Parameter of microcrystalline cellulose

Average Particle size analysis: Average particle size of HiCel™ microcrystalline cellulose was differentiated with different grades, it was shown in Table no.2 and HiCelTM 90 M average particle size (%) of three different batches were mentioned in table no.3.

Table No. 2 Particle size of different grade of HiCel ™ MCC

S.NO.	Grades Name	Particle Size (D50)
1	HiCel ™ 90M	100 µm
2	HiCel ™ 50M	50 µm
3	HiCel ™ LP200	170 µm
4	HiCel ™ XLM 90M	100 µm
5	HiCel ™ XLM 50M	50 µm

Bulk density

Untapped density: Bulk density of HiCel™ microcrystalline cellulose was found to be 0.29 to 0.30 g/cc.

Tapped density: Tapped density of HiCel™ microcrystalline cellulose was found to be 0.39 to 0.40 g/cc.

Table No.3. Physicochemical parameter tests of three different batches of HiCel™ MCC

S.No	Name of test	Batch no.		
		XXX_1	XXX_2	XXX_3
1	Yield (%)	90	92	92
2	Average particle size (%)	55	56	55
3	Untapped density (g/cc)	0.29	0.29	0.30
4	Tapped density (g/cc)	0.39	0.39	0.40
5	Hausner ratio	1.34	1.34	1.33
6	Angle of repose	39	38	39
7	Moisture content	3.98	4.00	4.00
8	pH	6.14	6.15	6.20
9	Conductivity	52	50	50
10	DOP	233	235	233
11	ROI (%)	0.056	0.056	.059
12	WSS (%)	0.13	0.13	0.14

Hausner's Ratio: Hausner ratio was presented the flow of powder, HiCel™ microcrystalline cellulose flow and hausner's ratio was reported 1.33 to 1.34.

Angle of repose: Angle of repose was represented the flow of powder. The flow ability of HiCel™ microcrystalline cellulose was very good; it was free flowing crystalline cellulose, Angle of repose was found to be 38° to 39°.

Moisture content: Moisture content of microcrystalline cellulose was found to be 3.98 to 4.00 %. In direct compression formulation less moisture content of tablets was achieved as good hardness and disintegration time.

pH: pH of HiCel™ microcrystalline cellulose was maintained between 6.14 to 6.20. It was acceptable in all industries such as formulation, food and cosmetics also.

Conductivity: The Conductivity of HiCel™ microcrystalline cellulose was found to be 50 to 52 µs/cm.

Degree of polymerization: Degree of polymerization of HiCel™ MCC was found to be 233 to 235. It was totally depend on

hydrolysis time, grade and types of wood pulp.

Residue on ignition: Residue on ignition of HiCel™ microcrystalline cellulose was found to be 0.056 to 0.059 % which was found in the range of 0.04 to 0.06 %.

Water soluble substances: Water soluble substances of HiCel™ microcrystalline cellulose was found to be 0.13 to 0.14 % which was found under the limits of IP not more than 0.2% and in USP not more than 0.25%.

Conclusion

Microcrystalline cellulose HiCel™ was spray dried cellulose; white crystalline, free flowing powder with excellent flow. Dissolving pulp was having very high MCC yield 87% to 92 %. It was found to be compatible for solid direct compression due to good properties of binding, lubrication and itself superdisintigrant.

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References

1. Kirsi Leooanen, Kari Pirakkalainen, Paavo Penttila, Jenni Sievanen, Nina Kotelnikova and Ritva Serimaa: Sami-angle x-ray scattering study on the structure of microcrystalline cellulose. Journal of Physics : Conference serious 2010; 247-249.
2. Shokri Javad and Adibkia Khosro: Application of cellulose and cellulose derivatives in pharmaceutical industries. Journal of INTECH open science 2013; 1:855-862.
3. Peter M.Fechner, Siegfried wartewig, Manfred Futing,andreas Helimann, Rennhard H.H, Neubert and Peter Kleninebudde: properties of microcrystalline cellulose and powder cellulose after extrusion/ spheronization as studied by fourier transform raman spectroscopy and environment scanning electron microscopy: AAPS Pharmasci 2003; 5:15-20.
4. IA, H.Nissan, Chapter 2: The pulp and paper marking processes: University park,PA: Pennsylvania state university 1981; 335-340.
5. Leppanen Kirsi, Seppo Andersson, Tarkkeli Mika, Matti Knaapila, Nina Kotelnikova, Ritava Serimaa: Structure of cellulose and microcrystalline cellulose from various wood species and flax studied by X-ray scattering: Journal of Springer Science + busnicess Media B.V.2009; 147-152.
6. Yakubu, A. Tanko, Mumar Sani S. D. Mohammed: Chemical modification of microcrystalline cellulose: improvement of barrier surface properties to enhance surface interaction with some synthetic polymers for biodegradable packing material processing and application in textile, food and pharmaceutical industry: Journal of Pelagia research library advance in applied research 2011; 2:532-540.
7. John Rojas, Alvin Lopez, Santiago Guisao and Carlos Ortiz: Evaluation of several microcrystalline cellulose obtained from agricultural by products. Journal of advanced pharmaceutical technology & research 2011; 1:170-185.
8. Terinte Nicoleta, Ibbett Roger and kurt Christian Schuster: Overview on native cellulose and microcrystalline cellulose structure studied by X-ray diffraction (waxd): Comparison between measurement techniques. Journal of Lenzinger Berichte 2011; 8:118-130.
9. Soppela Iral, Airaksinen Sari, Matti Murtomaa, Tenho Mikko, Juha Hatara, Heikki Raikkanen, Jouko Yliruusi, Niklas Sandler: Investigation of the powder flow behavior of binary mixtures of microcrystalline cellulose and paracetamol. Journal of excipient and food chem 2010; 1:55-67.
10. Staniforth, JN: Powder flow, in aulton ME (eds), Pharamaceutices – the science of

dosage form design. Churchill Livingstone, London, U.K. 2007;1045-1065.
11. Kumar Vijay, Sanjeev H. Kothari and Gilbert S. Banker: Compression, Compaction, and Disintegration Properties of Low Crystallinity Celluloses Produced Using Different Agitation Rates During their Regeneration from Phosphoric Acid Solutions. Journal of AAPS Pharma Science tech 2001; 1:245-250.
12. Jafar Ebrahimpour Kasmani, Mohammand Nemati, Ahmad Samariha, Hossein Chitsazi, Nima Seyed Mohammadi and ,Hassan Nosrati: Studing of effect of the age in Eucalyptus Camaldulensis species on wood chemical compounds used in pulping process. Journal of American-Eurasian J. Agric. & Environ Sci2011; 6:17-39.
13. Oyeniyi and Itiola, O.A: The physicochemical characteristic of microcrystalline cellulose, derived from sawdust, agriculture waste products. Journal of (Academic sciences) International journal of pharmacy and pharmaceutical sciences 2012; 1:196-200.
14. M.Nuruddin, A. Chowdhury, S.A. Haque, M.Rahman ,S.F.Farhad, M.Sarwar Jahan and A. Quaiyyum: Extraction and characterization of cellulose micrfibrils from agricultural wastes in an integrated biorefinery initiative. Journal of Cellulose chemistry and technology 2012; 1:17-20.
15. Necessitates in Remingtion: The science & practices of pharmacy. Editors Gennaro, A.R, Lippincott, Williams and Wilkins U.S.A.;1042-1052.
16. Babu S. Srekanth, Kumar A. Ajay, D.R. Suman: Co-Processed Excipients:A review. International journal of current trends in pharmaceutical research 2013; 3:70-75.
17. Martin: Physical pharmacy, Editors Alfred Martin, Pilar Bustamante & A.H.C. Chun, b.I. Waaverly pvt.ltd; 4:453-455.
18. The International Pharmacopeia 3rdedition: General method of analysis. WHO Publication 1979; 1:161-170.